Remarks

This amendment is responsive to the official action mailed September 22, 2004, and is accompanied by a Petition for Extension under 37 C.F.R. §1.136(a) and the required fee for a two month extension.

Claims 15-19 and 25-40 remain pending and under consideration, the remaining claims having been withdrawn from consideration as non-elected. The non-elected claims have now been canceled without prejudice to their presentation in a divisional application.

Among the claims remaining, the independent claims (15, 25 and 33) have each been amended to more particularly and distinctly define the subject matter of the invention and to more clearly distinguish over the prior art of record.

Claims 15 and 25 were rejected under 35 U.S.C. 102 as anticipated by Weaver, US Pat. 5,983,131, which is considered to disclose an electrode in contact with the human body, the electrode having a partially conductive outer surface. The remaining claims were rejected as obvious from Weaver in combination with other cited references. The examiner points out in the official action that the prior art does not teach the voltage and current values stated in applicant's claims, but takes the position that inasmuch as these values are determined by the human body tissues, arriving at them would be obvious.

Reconsideration is requested in view of the claims as amended. The prior art of record fails to disclose or suggest the invention defined by the amended claims as a whole.

Weaver teaches an externally applied contact-pad type electrode for electroporation treatment. Weaver's electrode only is "partially conductive" in the sense that the electrode contacts the tissue discontinuously. The electrode is patterned like a waffle iron or the like. However, the portion of the electrode that contacts the patient tissue in Weaver is conductive. There is no disclosure or suggestion that the electrode

could or advantageously should be only partially conductive. Weaver does not meet the invention claimed.

The claims as amended exclude the possibility of reading the term "partially conductive" as simply a matter of the spatial layout of the electrode. The claims recite an electrode with a conductive material within a partially conductive outer surface. This aspect of the invention is not disclosed in Weaver and is not obvious.

In Weaver, there is a distribution of areas on a contact pad that are placed for contact. For example at column 4, lines 32-48, the electrode can be a perforated plate (line 41). In such a structure, the perforations form spatial gaps in the conductive surface of the electrode. Other examples are a bar, a wire mesh, a plate with holes, etc. (See lines 45-46.) These are shapes for conductive electrodes and not electrodes having conductors behind a partially conductive surface layer or coating or similar structure.

The rejections under Sections 102 and 103 each rely on Weaver for the aspect of a "partially conductive" electrode. The claims have been amended to define the outer surface as the partially conductive element. This obviates the rejections over Weaver, which does not teach a partially conductive surface on a conductive electrode material. This aspect is particularly and distinctly defined in each of the independent claims and is not met by the prior art. Thus the invention is not shown to be anticipated as claimed, and there is no basis of record to assert that the invention claimed, as a whole, would have been obvious.

There is no teaching in Weaver that the surface of the electrode in contact with the tissue of the patient could or should have a partially conductive surface. Even if one assumes that materials are known that are more or less conductive, there is no reason to believe that it would be routine or obvious to face or surface an electrode with a material that is less than fully conductive. The primary object of an electrode is to make electrically conductive contact. It is counter-intuitive to suggest that decreasing the conductivity of an electrode would result in advantageous results.

The partially conductive surface of the electrodes employed as claimed is not simply an incidental matter, such as to render the surface of an electrode as in Weaver

more comfortable, e.g., warmer to the touch. Applicant's claims as amended define the electrode as penetrating or piercing a host tissue. Thus the matter of comfort or warmth is beyond the pale. Applicant's partially conductive coating serves to modify the electrical nature of the electrode, namely to limit the level of current applied to the tissue during the electroporation process.

For these reasons, the Weaver reference fails to disclose the invention as claimed. Weaver's electrode is conductive at all surfaces in contact with the patient. Weaver's waffle-iron electrode shape may provide a pattern of spaced areas of contact, but no limitation of conductivity is disclosed or suggested for the surfaces that contact the tissues of the patient/host. Whether one considers Weaver and the other references of record individually or in any routine combination, there is no basis to assert that applicant's invention as a whole would have been obvious.

The prior art of record discloses a number of infusion devices wherein the applicant of electrical energy to biological tissue is used to assist in moving a pharmaceutical agent through a biological barrier, especially through a cell wall. If the application of electrical power to tissue is entailed, it would be routine to attempt to apply such energy efficiently, including by obtaining good electrical contact with the tissues being treated. There is no suggestion in the prior art that there is anything to be gained by providing a surface on the electrode that is less conductive that it might be.

One might routinely believe from the prior art that the process of electroporation necessitates the application of a particular amount of electric power to the tissue being treated. Among the prior art references are various teachings of different levels of applied power. The power may be adjusted by varying the voltage level or the pulse repetition timing. However the prior art does not teach that a given level of applied power should advantageously be applied at a limited current level.

In connection with prior art devices that have a control circuit for adjusting the application of energy to the tissues, the control circuit may operate over some control range of voltage and current. The object is to apply the correct amount of electrical energy over the correct time profile to achieve the therapeutic purpose. If the control circuit is capable of controlling the power level and the time of exposure of the tissue to

the electric energy, then there would appear to be no reason, at least according to the prior art, for having a limitation on the conductivity of the contact between the electrode and the tissue.

In the rejection of claims 16-19 and 26-40 under Section 103, the examiner points out that Weaver does not disclose the step of measuring and recording current values, relying on the Flower reference for this aspect. Flower concerns a control arrangement wherein the voltage level is controllable, especially based on a sensed current level. The amount of electrical energy being applied is a matter of voltage and current, i.e., the power level is the mathematical product of voltage and current. If one seeks to achieve a particular therapeutic effect, one might assume that the power level is the critical aspect.

Also in the rejection under Section 103, the examiner asserts that the specific current and voltage levels are dictated by safety and the limitations of the human body, suggesting that the various voltage levels and current levels demonstrated by the prior art references of Dev et al., Lattin et al. and/or Webster show that applicant's voltage and current ranges are conventional.

Reconsideration is requested. Although applicant's disclosure and claims may state particular levels of applied voltage and delivered charge, these are recited as delivered via electrodes with partially conductive surfaces. There is no suggestion of this aspect in the prior art. Even assuming that the examiner is correct to say that one of the voltage and current parameters fits a given prior art range, the partially conductive character of applicant's electrode surface will cause the other of the respective current and voltage to have a very different value as compared to prior art electrodes that fail to interpose a partially conductive surface between the conductive body of the electrode and the tissue of the patient/host.

The prior art contains teachings of applying more or less electric power by using greater or lesser voltage or current levels over longer or shorter pulses. However, only applicant has determined that it is possible by limiting the conductivity of the surface of the otherwise conductive electrode, to improve the technique. Applicant has reduced the extent to which a penetrating electrode is conductively coupled to the host tissue, for

example the skeletal muscle of a human. Given a comparable power level and application time, applicant effectively has increased the extent to which the necessary electric power level (voltage times current) is applied as a voltage, and has reduced the extent to which the power is applied as a current.

A voltage drop occurs across applicant's conductive coating. However, an electrostatic field representing the full voltage drop occurs between the electrodes. The surface contact with the tissue is at a lower voltage and a lower current results. A higher voltage is placed in immediate proximity, namely in the conductive body of the electrode behind the partially conductive surface. This is a novel aspect by which the invention claimed as a whole patentably differs from the prior art.

The examiner's point is taken that the tissue determines the current that will flow at a given voltage. Other things being equal, the current that is produced in tissue between conductors contacting such tissue, at a given potential difference, is a function of the resistance of the tissue. However applicant has altered this arrangement by introducing a partially conductive coating on one or both electrodes. Thus the current produced in the tissue is reduced by the presence of the partially conductive coating.

One benefit of applicant's electrode with an only partially conductive outer surface is the limitation of patient discomfort and muscle spasms (electrically induced muscular contractions) that appear to be particularly associated with current). See paragraphs [0033], [0058], [0100], etc., of the published application.

Moreover, applicant's electrode arrangement also has been found to be effective, at least as compared to a conductive electrode arrangement . A comparison of test results achieved is shown in applicant's Table I, particularly comparing Groups 1 to 3, which include conditions where current is limited as claimed, versus closely coupled conductively to the tissue.

Applicant's claims as amended particularly define the partially conductive surface of the electrodes for application to host tissues generally, and thus patentably distinguish from the prior art. Furthermore, new claims 41-43 are limited to methods involving skeletal muscle tissue. In the application of electrical power for electroporation, it may be desirable to apply power specifically to skeletal muscles

infused with an agent. (See, e.g., Mathiesen and Dev references, of record). Applicant advantageously applies power to patient/host tissues and limits current levels. This aspect is not found or suggested by the prior art, including the references that specifically mention skeletal muscle as apt for electroporation.

Skeletal muscle tissue in particular is inhomogeneously striated, leading to localization of conductive paths that may aggravate the tendency toward electrically induced spasms and associated discomfort. However skeletal muscles also have been found to be an effective site for electroporation in association with efforts to invoke certain immune responses. Applicant has developed a technique of altering the conventional direct coupling of conductive electrodes to tissues, limiting the applied current in the manner claimed, namely by interposing an only partly conductive coating, e.g., a resistive, dielectric or otherwise partially conductive material.

The disclosure and claims are in proper form. The claims have been amended to particularly and distinctly define the subject matter regarded as the invention. The claims as amended clearly distinguish over the prior art of record. The differences between the invention and the prior art are such that the subject matter claimed, as a whole, is not shown to have been known or obvious. Therefore, the application is in condition for allowance. Reconsideration and allowance are requested.

Respectfully submitted,

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